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14. In addition to developmental studies to determine whether normal contacts existed initially, it is essential to perform studies to determine whether the lack of noradrenergic varicosities is the result of a peptide deficiency or merely the result of an increased turnover rate in the terminals as a result of chronic dehydration.
15. These data were determined by dividing the SON into dorsal and ventral regions representing oxytocin- and vasopressin-rich regions, respectively, as determined with immunohistochemical techniques in normal rats and verified with neurophysin staining in the homozygous Brattleboro rat (*11*).
16. We thank J. Fields for skilled technical assistance. Antiserum to rat neurophysin was provided by A. G. Robinson through PHS grant AM 16166. This work was supported by PHS grants NS 15816, AG 00847, and MH 14577.
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Oculomotor Reaction Time in Dementia Reflects Degree of Cerebral Dysfunction

Abstract. *The effects of diffuse cerebral dysfunction on oculomotor reaction time were assessed in patients with dementia of presumed Alzheimer's etiology and in normal age-matched control subjects. Patients were classified into mild, moderate, and severe groups on the basis of independent neurological, neuropsychological, and neuroradiological ratings for disease severity. Saccadic latencies to targets appearing in parafoveal and near peripheral vision showed significant increases from the normal controls to dementia groups, with each severity subdivision clearly differentiated from the others in terms of mean oculomotor reaction time. These data offer strong evidence for a direct relationship between degree of cortical structural integrity and simple oculomotor reaction time and suggest a higher cortical regulatory role in sensory-motor integration.*

For more than 130 years, reaction time (RT) has been examined experimentally as a measure of conduction speed of the central nervous system. As early as 1850, Helmholtz (*1*) used an RT measure to estimate the speed of transmission along a frog's motor nerve. Reaction time has been used as an index of cerebral dysfunction in a variety of brain-damaged groups, with latencies exceeding normal values (*2–5*). Prolonged RT's on both the ipsilateral and contralateral side in patients with unilateral cerebral disease (*4*) suggest that RT may reflect the degree of overall cerebral intactness rather than specify localized damage. Correlations of RT to severity of brain injury or dysfunction (*5*) argue further for an association between this simple sensory-motor task and the extent of involvement of the central nervous system's cortical substrate. Our study examined the relationship between RT performance and the severity of dementia (and by inference, cerebral integrity) in patients with presumed dementia of the Alzheimer's type (DAT) (*6*).

Such dementia (*7*) is marked by progressive cerebral degeneration of unknown etiology, producing cognitive and psychomotor disturbances. Alzheimer's is believed to be the most frequent cause of dementia (*8*). Morphologically, DAT is characterized by ventricular dilation and cortical atrophy most prominent in the frontal and temporal lobes. Microscopically, the degenerative changes include senile plaque formation, neurofibrillary tangling, and granulovacuolar degeneration.

Simple oculomotor RT was chosen as the experimental measure because this task minimizes attentional and vigilance factors, since short saccades to stimuli have been traditionally considered volitional but highly automated (*9*). Oculomotor RT of 12 normal age- and sex-matched elderly control subjects and 12 patients with DAT were obtained (*10*). The DAT patients were further divided into mild, moderate, and severe groups (four per group) on the basis of independent neurological, neuropsychological, and neuroradiological ratings for disease severity. A deterioration index derived from these separate evaluation procedures consisted of the average ranking on these severity scales (from 1, minimum impairment, to 5, severe impairment) (*11*).

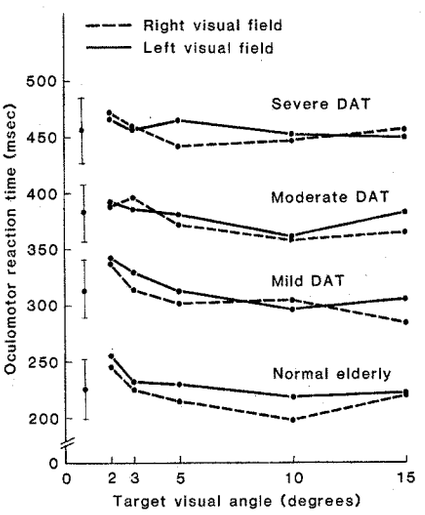

Fig. 1. Group mean oculomotor RT's as a function of visual angle and visual half-field. Means (± standard deviations) across target visual angles and visual fields are shown at the left.

Saccadic latencies were obtained with an eye-movement recorder (Biometric model 200) paired with a digital processor (Nova 12/20). Three-letter consonant-vowel-consonants (CVC's) displayed on a cathode-ray tube (CRT) (Lexiscope) served as the stimuli. The CVC's in the right visual field had the first letter beginning at a visual angle of 2°, 3°, 5°, 10°, or 15°, with the last letter of the CVC ending at similar angles in the left field trials. All stimuli subtended 1° of horizontal visual angle and were displayed for 1 second. A short practice and calibration session for the photoelectric sensors preceded the actual experimental session. Eight trials at each of the ten positions presented in a random sequence (sampling without replacement) constituted the experimental session. Each subject rested his head in a chin and forehead rest with the glabella 40 cm away from the CRT. We initiated trials with a "ready" command when subjects were fixated on the zero point on the CRT. Subjects were instructed to move their eyes to the location of the stimulus and name the word. Oculomotor RT was defined as the interval between stimulus onset and time of movement to the appropriate half-field of 0.5°, an experimentally determined value used to separate target saccadic movements from ongoing oscillatory eye jitter. Latency windows of 100 to 400 msec for normal subjects and 100 to 1000 msec for patients were used to accept saccadic RT values; approximately 4 percent of normal subjects' and 8 percent of DAT patients' trials fell outside these limits and were not analyzed. Eye position was sampled at 1000 points per second for the 1-second period after stimulus onset.

Data analyses were based on subject median RT values, as some tendency to positive skewing was evident in the patient group. The overall latency of the DAT patients was 158 msec longer than that of the normal aged controls (Fig. 1). Analyses of variance (*12*) demonstrated that DAT patients displayed significantly ($P < .001$) longer saccadic latencies than normal subjects and that the mild, moderate, and severe groups in turn had significantly ($P < .001$) different latencies from one another. Group separation

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remained relatively constant at all target presentation sites, with no interactions found between group and visual angle or half-field.

Both the patients and the normal subjects showed progressively decreasing latencies as stimuli moved farther into the periphery with the exception of the 15° condition, where RT increased (*13*). Eye movements to targets in the right visual field had significantly shorter latencies (9 msec) than leftward saccades. This observation is in agreement with other studies finding this perceptual motor asymmetry. A structural basis underlies this oculomotor asymmetry, since only dextrals show a significant rightward advantage (*14*). All subjects in our study were right-handed as determined by a hand-preference questionnaire. The interaction of saccadic latency asymmetry with handedness supports the hypothesis of cortical modulation of oculomotor RT (*15*).

Spooner *et al.* (*16*) have demonstrated that older normal subjects have (i) significantly decreased eye movement velocities during saccadic and pursuit testing, (ii) increased latency in the slow component of optokinetic nystagmus, and (iii) an increase in saccadic RT of about 40 msec over normal younger subjects. We have previously shown that saccadic latency decreases through childhood into young adulthood (from approximately 212 msec to 179 msec in young adults) (*3, 15*).

A number of well-documented peripheral and central changes specific to the human visual system could be responsible for age-related declines in visual and oculomotor function (*17*). Alternatively, numerous more generalized morphological changes have been described in the normal aging nervous system (*18*), which could underlie deficits in sensory and motor information processing and contribute to this RT difference. An essential qualitative similarity has been proposed between morphological changes in the central nervous system during aging and Alzheimer's disease (*19*). While advancing age was associated with a modest increase in oculomotor RT in our study, the presence of diffuse cerebral pathology in DAT greatly disrupted saccadic latencies. Furthermore, clinically assessed severity, with the concomitant assumption of correlated cortical structural alterations, has a profound influence on oculomotor RT. This effect is larger than normal age-related changes, since the oculomotor RT increases from normal young adult to normal elderly were roughly half of the stepped increases between mild, moderate, and severe DAT groups.

Despite the relationship between clinical signs and symptoms of dementia and the noninvasive imaging of the degree of cerebral involvement, our study does not provide direct evidence for a causal relationship between the morbid anatomy and disturbance in this simple visual-motor function. Several studies (*20*) have shown a positive correlation between neuropsychological sequelae and neuroanatomical features of DAT, but further investigation is required to determine whether a specific causal link exists between the cortical degenerative changes in Alzheimer's disease and the disturbances of intellectual and psychomotor function.

Reaction time provides a reliable psychological measure of the speed of discrete neurophysiological events. A common view of functional components in simple RT has been that performance requires perception and registration of an incoming sensory stimulus, motor response translation, decisional processes, and motor execution. In the oculomotor RT paradigm, this intermediate stage has a more automated, involuntary characteristic than in RT tasks involving distal upper or lower extremity responses. Our subjects found it most difficult to maintain fixation and avoid eye movements, despite instructions to do so, when objects appeared in their parafoveal and near peripheral vision. That such an automated sensory motor function as oculomotor RT should be affected by the degree of structural cortical integrity may suggest an overall cortical toning or regulatory descending influence on lower centers involved in saccadic motor execution. The sensitivity of simple oculomotor RT to presumed neuropathophysiological status supports the hypothesis that RT performance accesses a cardinal functional dimension of the central nervous system.

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12. Normal aged versus combined DAT subjects: latency was increased for patients [$F(1, 22) = 70.26$, $P < .001$], for left visual field presentation [$F(1,22) = 10.10$, $P < .01$], and for stimulus presentation at visual angles nearest the point of fixation [$F(4,88) = 14.84$, $P < .001$]. No higher order significant interactions were found among these variables. The effects of disease severity were examined in an additional analysis of variance with the three severity groups contrasted as the between-subjects factor. Increased disease severity based on the deterioration index was associated with significantly longer saccadic latencies [$F(2, 9) = 179.88$, $P < .001$]; Newman-Keuls multiple comparisons among the three group means demonstrated that the mild group displayed significantly ($P < .001$) shorter oculomotor RT's than the moderate group, which in turn had significantly ($P < .001$) shorter RT's than the severe group.
13. Post hoc comparisons were conducted with the Newman-Keuls test on the visual angle means to

determine the sources of significance in this main effect. Stimuli at 2° yielded significantly ($P < .01$) increased latencies over each of the other visual angles, while both 3° ($P < .01$) and 5° ($P < .05$) presentations were significantly increased over the 10° conditions. Stimuli presented at 15° produced significantly ($P < .05$) longer latencies than those at 10°. A similar bimodal relationship has been hypothesized to support different visual programming systems according to location of targets in visual space [D. Frost and E. Poppel, *Biol. Cybern.* **23**, 39 (1976); F. J. Pirozzolo and K. Rayner, *Neuropsychologia* **18**, 224 (1980)].
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Ureterosigmoidostomy and Colon Carcinogenesis

Although Crissey *et al.* (*1*) have devised a successful model for ureterosigmoidostomy in the rat, we advocate caution in accepting their hypothesis that the resulting anastomotic tumors are caused by urinary enzymes activating fecal procarcinogens. The authors overlooked the tendency for almost any intestinal anastomosis to be a favored site for tumor formation, both in man and experimental animals (*2*). Spontaneous intestinal tumors in rodents are rare (*3*), but we (*4*) encountered one adenocarcinoma at a colonic transection site in a rat receiving no carcinogen, and a similar phenomenon occurred in Crissey *et al.*'s (*1*) experiment. Since some of the intestinal carcinogen employed (dimethylhydrazine) reaches the colonic mucosa through the bloodstream (*5*), the absence of tumors at the suture line after proximal diverting colostomy probably reflects the colonic atrophy of defunction (*6*). Chemical carcinogenesis in the distal colon is reduced, though not abolished, by proximal colostomy (*7*).

We suggest that the development of tumors at sites of intestinal anastomosis is more likely to result from hyperplasia provoked by surgical trauma or the presence of suture material. Indeed, compensatory postresectional hyperplasia, which may be maximal in the immediate vicinity of an anastomosis (*8*), probably accounts for enhanced carcinogenesis after intestinal resection in experimental animals (*2*). In the experiment of Crissey and his colleagues, the specific effect of urinary diversion might have been tested by performing sigmoid colotomy or transection rather than vasectomy as the control operation.

Until some of these etiologic uncertainties are resolved, it is premature to conclude that the use of colon conduits in children is entirely free from the risk of subsequent carcinoma.

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Bristol and Williamson raise a valid question as to the role of a colonic suture line in carcinogenesis. However, we found that neither a sutured colostomy (0/10) nor the anastomosis to the colon of a vascularized patch of bladder without urinary inflow (0/13) had any tumors after 1 year (*1*). These controls clearly could not suffer from "atrophy of defunction." The required presence of urine and feces for tumor formation leads us to our currently favored hypothesis that the obligatory urinary precarcinogens (for example, nitrate) become activated to short-lived proximate carcinogens by fecal bacteria. The phenomenon of suture-line sensitization to carcinogens brought up by Bristol and Williamson may well provide the explanation for the consistent location of the resulting bowel tumors at the suture line.

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Plankton Productivity and the Distribution of Fishes on the Southeastern U.S. Continental Shelf

The report by Turner *et al.* (*1*) is an important contribution to a topic that is becoming increasingly popular (*2*). However, the conclusions in (*1*) could have benefited from additional sources of data which bear significantly on the results. I believe that the winter increase in offshore primary productivity shown in figure 2 of (*1*) is also an important component of nearshore shelf coupling. In the South Atlantic Bight there are generally two periods of annual abundance associated with the spawning of nearshore marine and estuarine species. A summer and early fall peak is associated with the presence of primarily anchovies (Engraulidae) and gobies (Gobiidae). This peak seems to coincide with the one shown in figure 2 of (*1*). As Turner *et al.* suggested, many individual eggs and larvae may have been washed out of local estuaries.

A second peak of seasonal abundance, however, normally occurs in winter and early spring and is coincident with the spawning of spot (*Leiostomus xanthur-*

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